Journal of Neonatal Surgery
ISSN(Online): 2226-0439
Vol. 14, Issue 30s (2025)
https://www.jneonatalsurg.com

OPEN ACCESS

Comparison of Myocardial Protection Effects Between Enriched Crystalloid Cardioplegia Solution and St. Thomas Solution: An Experimental Study on Oryctolagus cuniculus

Aditya Rahman[1,2], Yan Efrata Sembiring[1,2], Dhihintia Jiwangga Suta Winarno[1,2]

[1]Departemen of Thoracic, Cardiac, and Vascular Surgery, Faculty Medicine, UNIVERSITAS AIRLANGGA, Surabaya

[2]Departemen of Thoracic, Cardiac, and Vascular Surgery, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia

Email ID: adityarahmandito@gmail.com; Email ID: aditya.rahman-2021@fk.unair.ac.id;

Email ID: dhihintiajiwangga@yahoo.com

[3]School of Clinical Medicine, Youjiang Medical University for Nationalities, Baise, China.

Email ID: 298750007@qq.com

[4]The First School of Clinical Medicine, Guangxi University of Science and Technology,Liuzhou, China.

Email ID: 3143357226@qq.com

[5]Center for Educational Assessment and Teacher Development, Youjiang Medical University for Nationalities, Baise, China.

Email ID: yyixia@163.com

[*]Corresponding author:

Yan Efrata Sembiring

Email ID: yan-e-s@fk.unair.ac.id

Cite this paper as: Aditya Rahman, Yan Efrata Sembiring, Dhihintia Jiwangga Suta Winarno, (2025) Comparison of Myocardial Protection Effects Between Enriched Crystalloid Cardioplegia Solution and St. Thomas Solution: An Experimental Study on Oryctolagus cuniculus. *Journal of Neonatal Surgery*, 14 (30s), 480-484.

ABSTRACT

Background: Cardioplegic solutions are critical for myocardial protection during cardiac surgery. Enriched Crystalloid Cardioplegia (ECC), modified from the St. Thomas solution with added mannitol, $MgSO_4$, and lidocaine, may enhance protection. This study conducted to compare the myocardial protection efficacy of ECC and St. Thomas solution in rabbits during ischemia

Methods: Eighteen male *Oryctolagus cuniculus* rabbits were randomized into three groups (n=6 each): ECC, St. Thomas, and control (Ringer Lactate). Cardioplegia was administered via antegrade aortic root infusion (15 mL/kg, 25°C, single dose). After 90 minutes of aortic cross-clamping, myocardial tissues were collected at 30, 60, and 90 minutes for histological evaluation using H&E staining. Outcome measures included myocardial injury score, extent of damage, and neutrophil infiltration.

Results: ECC showed significantly lower injury scores at 30 and 60 minutes compared to control ($p= 0.027$ & $p= 0.018$). No significant difference was found between ECC and St. Thomas. At 90 minutes, differences were not statistically significant. No significant differences were observed in infarct size or neutrophil infiltration between groups.

Conclusion: ECC offers myocardial protection comparable to St. Thomas solution, with a trend toward prolonged efficacy. Its additional agents may enhance protective mechanisms during cardiac arrest.

Keywords: *Enriched Crystaloid Cardioplegia, myocardial protection, rabbit model*

1. INTRODUCTION

Cardiac surgical procedures requiring cardiopulmonary bypass often necessitate aortic cross-clamping and cardioplegic arrest. While these steps are essential to ensure a motionless operative field and myocardial protection, they also pose a risk of ischemia-reperfusion injury. Cardioplegia plays a critical role in reducing myocardial oxygen demand, halting electrical activity, and minimizing metabolic stress [1,2].

The St. Thomas solution has long been a standard for myocardial protection due to its well-established efficacy and availability. However, its relatively short duration of action have driven exploration of alternative formulations. Enriched

Crystalloid Cardioplegia (ECC) was developed as a modified version of St. Thomas, enhanced with additional agents such as mannitol, magnesium sulfate ($MgSO_4$), and lidocaine—components that may augment myocardial protection through antioxidative, anti-inflammatory, and antiarrhythmic mechanisms. This study aims to compare the myocardial protective effects of ECC and St. Thomas solution using a rabbit model.

2. METHODS

This experimental in vivo study was conducted with ethical approval from the Animal Care and Use Committee, Faculty of Veterinary Medicine, Universitas Airlangga (No: 2.KEH.167.11.2024). A total of 18 male New Zealand White rabbits (*Oryctolagus cuniculus*), aged 1–2 years and weighing 3–4 kg, were selected.

Animals were randomly assigned into three groups (n=6 per group): ECC group, St. Thomas group, and control group receiving Ringer Lactate. Group A (ECC): KCl (37.5 mEq/L), $NaHCO_3$ (25 mEq/L), mannitol 20% (10 mL), $MgSO_4$ 20% (12.5 mL), and lidocaine 2% (6 mL). Group B (St. Thomas): NaCl (144 mEq/L), K (16 mEq/L), Ca (1.2 mEq/L), and Mg (16 mEq/L). Group C (Control): Ringer Lactate. Each solution was administered via antegrade aortic root delivery at 25°C, in a volume of 15 mL/kg over 2–4 minutes. No cardiopulmonary bypass was used, and the aorta was cross-clamped for 90 minutes.

At 30, 60, and 90 minutes post-clamping, myocardial tissue samples were collected for histological analysis using hematoxylin and eosin staining. Three histopathological scoring systems were employed. First, the tissue injury score assessed morphological damage on a scale from 0 to 5: a score of 0 indicated normal myocardium; 1 represented patchy eosinophilic changes; 2 denoted localized hemorrhagic changes with eosinophilic foci; 3 indicated localized necrosis; 4 reflected diffuse hemorrhage and eosinophilia; and 5 corresponded to diffuse liquefaction necrosis. Second, the extent of myocardial damage quantified the percentage of left ventricular (LV) infarction: score 0 corresponded to <30% infarction, score 1 to 30–50%, and score 2 to >50%. Lastly, the neutrophil infiltration index was determined by calculating the average number of neutrophils observed in five high-power fields (400× magnification), reflecting the degree of acute inflammatory cell infiltration.

Normality was tested with the Shapiro-Wilk test. Comparative analyses used Kruskal-Wallis, Mann-Whitney U, and one-way ANOVA as appropriate. A p-value <0.05 was considered statistically significant.

3. RESULTS

Histological Myocardial Injury Score

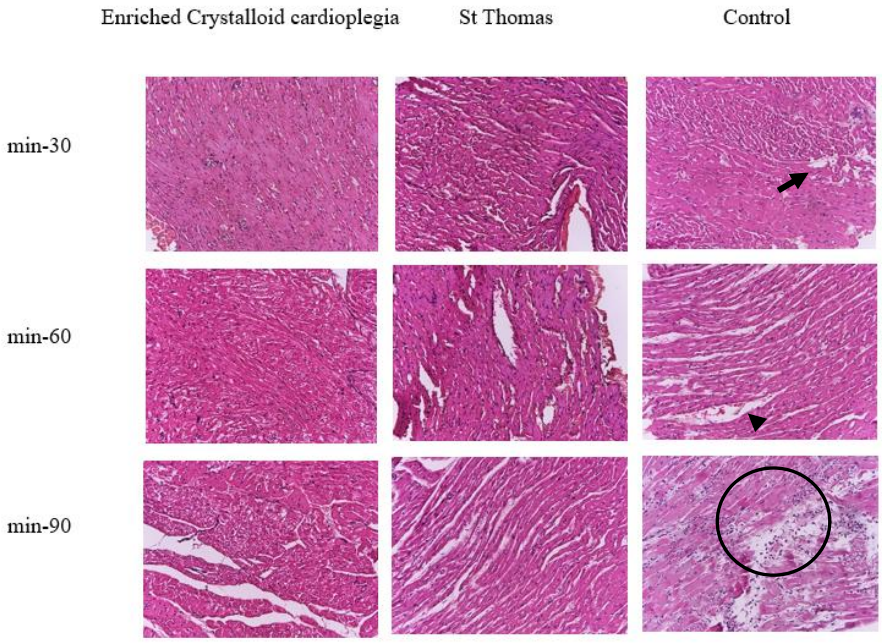

Fig. 1. Histopathological appearance of myocardial tissue (H&E 200×). Arrow: mild disorganization of myocardial fibers and widening of intercellular spaces. Arrowhead: more severe structural disorganization, noticeable cellular swelling, and inflammatory cell infiltration. Circled area: extensive tissue damage characterized by loss of muscle fiber architecture, cellular necrosis, dense inflammatory infiltration, and widespread interstitial edema.

This study demonstrates that Enriched Crystalloid Cardioplegia (ECC) provides a myocardial protective effect comparable to the widely used St. Thomas solution, particularly within the first 60 minutes of ischemia (Table 1). At both 30 and 60 minutes, overall group differences in injury scores were statistically significant (p = 0.018 and p = 0.025, respectively, Kruskal–Wallis). Post-hoc pairwise comparisons revealed that ECC significantly reduced myocardial injury compared to the control group at both time points, and St. Thomas also significantly outperformed the control. No significant differences were observed between ECC and St. Thomas at any time point.

By 90 minutes, however, no statistically significant differences were observed among the groups, highlighting the limitation of single-dose cardioplegia over extended ischemia durations. This finding emphasizes the importance of cardioplegia redosing or the incorporation of a reperfusion phase in prolonged surgeries.

Table 1. Myocardial Injury Scores by Group and Time

Group	Myocardial injury				*p (Kruskal-Wallis)*	*p (Mann-Whitney)*
	Score 0	Score 1	Score 2	Score 3		
min-30						ECC vs Control
ECC	4	2	0	0	0,018*	(p = 0,027*)
St Thomas	5	1	0	0		St Thomas vs Control
						(p = 0,014*)
Control	1	1	4	0		ECC vs St Thomas (p = 0,523)
min-60						ECC vs Control
ECC	3	2	1	0	0,025*	(p = 0,018*)
St Thomas	2	3	1	0		St Thomas vs Control
						(p = 0,022*)
Kontrol	0	1	4	1		ECC vs St Thomas
						(p = 0,665)
min-90						
ECC	0	3	2	1	0,164	
St Thomas	0	2	1	3		
Control	0	0	2	4		

Extent of Myocardial Damage

Table 2. Comparative Assessment of Myocardial Infarction Extent Following Cardioplegia

Group	Extent of damage				*p (Kruskal-Wallis)*
	Score 0	Score 1	Score 2	Score 3	
Min-30					
ECC	4	2	0	0	0,263
St Thomas	5	1	0	0	
Control	1	5	0	0	
Min-60					
ECC	3	2	1	0	0,109
St Thomas	2	2	2	0	

Control	0	2	4	0	
Min-90					
ECC	0	3	2	1	0,263
St Thomas	1	2	2	1	
Control	0	1	2	3	

Unlike the histopathological injury scores, the extent of myocardial damage—as evaluated by infarct area—did not show statistically significant differences among the groups at any time point. At 30 minutes, the ECC and St. Thomas groups demonstrated fewer severe infarctions compared to the control group, but these differences were not statistically significant. This pattern remained consistent at 60 and 90 minutes.

Neutrophil Infiltration Index

Table 3. Neutrophil Infiltration Scores in Myocardial Tissue Following Cardioplegia Administration

Group	**Mean ± SD**	***p*** *(one-way ANOVA)*
ECC	4,83 ± 1,94	0,565
St Thomas	6,33 ± 2,42	
Control	6,00 ± 3,03	

Histological quantification of neutrophil infiltration in myocardial tissue revealed no statistically significant differences among the three groups. Although the ECC group showed numerically lower neutrophil counts compared to the St. Thomas and control groups, the variation was not sufficient to reach statistical significance.

4. DISCUSSION

The present study demonstrates that ECC offers myocardial protection comparable to the standard St. Thomas solution. Both solutions significantly reduced histological signs of myocardial injury compared to the control. At 30 and 60 minutes, ECC and St. Thomas groups had lower injury scores, with ECC showing a slight, though not statistically significant, trend toward better preservation.

The addition of mannitol in ECC is hypothesized to reduce myocardial edema and scavenge free radicals, thereby reducing oxidative stress. Mannitol acts as an osmotic diuretic, pulling fluid out of cells and limiting cellular swelling. Studies have shown that mannitol attenuates reperfusion injury and supports mitochondrial function [6,7].

Magnesium sulfate in ECC helps by blocking calcium channels and stabilizing cellular membranes. Calcium overload is a known contributor to reperfusion injury, leading to hypercontracture and cell death. By limiting calcium influx, magnesium reduces cellular injury and postoperative arrhythmias [8].

Lidocaine contributes antiarrhythmic and membrane-stabilizing effects. It prolongs myocardial refractory periods and reduces sodium and calcium influx during ischemia. Studies support its role in reducing defibrillation needs and improving spontaneous rhythm restoration [9].

Although there were no significant differences in infarct size or neutrophil infiltration, this may be attributed to the relatively short duration of ischemia or the inherent limitations of crystalloid cardioplegia compared to blood-based solutions.

5. CONCLUSION

ECC shows promising early myocardial protective effects, likely enhanced by its additive agents. While differences in infarct size and inflammation were not significant, trends toward better preservation suggest that ECC may offer benefits over St Thomas solution, particularly in short to moderate ischemic periods. Future studies incorporating longer ischemic durations and biochemical markers will be essential to further define its clinical potential.

REFERENCES

[1] Chambers DJ, Fallouh HB. Cardioplegia: the developing science of myocardial protection. Eur J Cardiothorac Surg. 2010;38(3):219–29.

[2] Glöckner A, Böttiger BW, Meinhardt A. Myocardial protection in cardiac surgery. J Thorac Dis. 2021;13(6):3984–4002.

[3] Zhu X, et al. Myocardial histological injury scoring. J Mol Cell Cardiol. 2002;34(3):233–9.

[4] Bayat P, et al. Histopathologic scoring of myocardial infarction. Cardiovasc Pathol. 2002;11(1):21–8.

[5] Mueller M, Klinke A, David S, et al. Evaluation of neutrophil infiltration in myocardial tissue using immunohistochemical techniques. J Mol Histol. 2017;48(4):289–96.

[6] Sanetra K, et al. Mannitol in myocardial protection: antioxidant and osmotic effects. Thorac Cardiovasc Surg. 2018;66(1):20–8.

[7] Ferreira R, et al. Mannitol improves myocardial mitochondrial preservation during ischemia. J Thorac Cardiovasc Surg. 1989;98(3):530–7.

[8] Shakerinia M, et al. Magnesium in cardioplegia and its myocardial effects. Ann Thorac Surg. 1996;61(5):1323–30.

[9] Ahmed A, et al. Meta-analysis of Del Nido cardioplegia: efficacy of lidocaine and magnesium. J Card Surg. 2024;39(1):13–22.